

What is Claimed:

1. A biologically active, fibrin microbead comprising extensively cross-linked fibrin(ogen).

2. The fibrin microbead of Claim 1, wherein at least 30% of the fibrin(ogen) is cross-linked.

3. The fibrin microbead of Claim 1, wherein at least 50% of the fibrin(ogen) is cross-linked.

4. The fibrin microbead of Claim 1, wherein the fibrin(ogen) is cross-linked as shown in Figure 3D.

5. The fibrin microbead of Claim 1, having a diameter of about 50-200 microns.

6. The fibrin microbead of Claim 1, which further comprises at least one bioactive agent.

7. A method for producing fibrin microbeads comprising the steps of: (i) preparing an aqueous solution comprising fibrinogen, thrombin and Factor XIII; (ii) prior to the onset of coagulation, introducing the aqueous solution into an oil heated to a temperature of about 50-80°C to form an emulsion; (iii) mixing the emulsion at a temperature of about 50-80°C until fibrin microbeads comprising extensively cross-linked fibrin(ogen) are obtained; and (iv) isolating the fibrin microbeads.

8. The method of Claim 7, wherein the aqueous solution comprising fibrinogen, thrombin and Factor XIII is prepared by combining purified fibrinogen containing endogenous Factor XIII with thrombin.

9. The method of Claim 7, wherein the aqueous solution comprising fibrinogen, thrombin and Factor XIII is

prepared by combining cryoprecipitate containing endogenous fibrinogen and endogenous Factor XIII, with thrombin.

10. The method of Claim 7, wherein the aqueous solution comprising fibrinogen, thrombin and Factor XIII is prepared by combining fibrinogen, Factor XIII and thrombin.

11. The method of Claim 7, wherein ratio of fibrinogen:thrombin:Factor XIII in the aqueous solution is 5-100 mg/mL:1-100 U/mL:1-50 U/mL.

12. The method of Claim 7, wherein ratio of fibrinogen:thrombin:Factor XIII in the aqueous solution is 20-40 mg/mL:5-10 U/mL:2-20 U/mL.

13. The method of Claim 7, wherein the aqueous solution further comprises at least one bioactive agent.

14. The method of Claim 7, wherein the aqueous solution containing fibrinogen, Factor XIII and thrombin is introduced into the oil within about 30 seconds after preparing the aqueous solution.

15. The method of Claim 7, wherein the oil is selected from the group consisting of vegetable oils, petroleum based oils, silicone oils, and combinations thereof.

16. The method of Claim 15, wherein the oil is a vegetable oil selected from the group consisting of corn oil, olive oil, soy oil, coconut oil, and combinations thereof.

17. The method of Claim 16, wherein the vegetable oil is corn oil.

18. The method of Claim 7, wherein the oil is admixed with a hydrophobic organic solvent.

19. The method of Claim 18, wherein the organic solvent is isooctane.

20. The method of Claim 7, wherein the emulsion is mixed for about 3-9 hours.

21. The method of Claim 7, wherein the fibrin microbeads are isolated by centrifugation, filtration, or a combination thereof.

22. The method of Claim 7, which further comprises grading the isolated microbeads to the desired size.

23. A composition comprising cells bound to fibrin microbeads, wherein the microbeads are biologically active and comprise extensively cross-linked fibrin(ogen).

24. The composition of Claim 23, wherein the cells are selected from the group consisting of fibroblasts, endothelial cells, chondrocytes, neuroblastoma cells, kidney cells, liver cells, pancreatic cells, thyroid cells, glial cells, smooth muscle cells, mouse mammary carcinoma cells, bone/cartilage forming cells, and combinations thereof.

25. The composition of Claim 23, wherein the fibrin microbeads further comprise at least one bioactive agent.

26. The composition of Claim 23, wherein the cells are infected with a virus.

27. The composition of Claim 23, wherein the cells express a recombinant protein.

28. The composition of Claim 23, wherein the cells contain exogenous nucleic acid.

29. A method for culturing cells comprising the step of: culturing fibrin microbead binding cells with fibrin

microbeads in a culture medium under conditions permitting the cells to bind to the fibrin microbeads, wherein the microbeads are biologically active and comprise extensively cross-linked fibrin(ogen).

30. The method of Claim 29, wherein the fibrin microbead binding cells are selected from the group consisting of fibroblasts, endothelial cells, chondrocytes, neuroblastoma cells, kidney cells, liver cells, pancreatic cells, thyroid cells, glial cells, smooth muscle cells, mouse mammary carcinoma cells, bone/cartilage forming cells, and any combination thereof.

31. The method of Claim 29, which further comprises the step of isolating the fibrin microbeads from the culture medium.

32. The method of Claim 29, wherein the fibrin microbeads further comprise at least one bioactive agent.

33. The method of Claim 29, wherein the cells are infected with a virus.

34. The method of Claim 33, which further comprises the step of isolating the virus from the cell culture.

35. The method of Claim 29, wherein the cells produce a recombinant protein.

36. The method of Claim 35, which further comprises the step of isolating the recombinant protein from the cell culture.

37. The method of Claim 29, wherein the cells contain exogenous nucleic acid.

38. The method of Claim 37, which further comprises the step of isolating the exogenous nucleic acid from the cell culture.

39. A method for separating cells that bind to fibrin microbeads from a cell culture containing the fibrin microbead binding cells and cells that do not bind to fibrin microbeads, said method comprising the steps of: (i) culturing the cell culture with fibrin microbeads in a culture medium under conditions permitting the fibrin microbead binding cells to bind to the fibrin microbeads, wherein the microbeads are biologically active and comprise extensively cross-linked fibrin(ogen), and (ii) isolating the fibrin microbeads from the culture medium.

40. The method of Claim 39, wherein the fibrin microbead binding cells are selected from the group consisting of fibroblasts, endothelial cells, chondrocytes, neuroblastoma cells, kidney cells, liver cells, pancreatic cells, thyroid cells, glial cells, smooth muscle cells, mouse mammary carcinoma cells, bone/cartilage forming cells, and combinations thereof.

41. A method for transplanting desired cells in a patient comprising preparing a composition comprising cells bound to fibrin microbeads, wherein the fibrin microbeads are biologically active and comprise extensively cross-linked fibrin(ogen), and transplanting the composition into the patient.

42. The method of Claim 41, wherein the cells are wound healing promoting cells and are transplanted into a wound of the patient.

43. The method of Claim 42, wherein the wound healing promoting cells are selected from the group consisting of fibroblasts, endothelial cells, chondrocytes, bone/cartilage forming cells and combinations thereof.

44. The method of Claim 42, wherein the fibrin microbeads further comprise at least one bioactive agent selected from the group consisting of wound healing promoting agents, growth factors, glucocorticosteroids, steroids, antibiotics, antibacterial compounds, antiviral compounds, and antifungal compounds.

45. The method of Claim 42, wherein the composition is affixed to the wound using fibrin glue.

46. The method of Claim 41, wherein the cells express a protein in an amount sufficient to treat a disease associated with a deficiency in the protein so expressed.

47. A method for engineering tissue comprising the steps of: (i) preparing a suspension of desired cells bound to fibrin microbeads, wherein the fibrin microbeads are biologically active and comprise extensively cross-linked fibrin(ogen); (ii) applying the suspension to the surface of a prosthetic device; and (iii) culturing the cells in a tissue culture medium under conditions permitting the formation of tissue on the surface of the prosthetic device.

48. The method of Claim 47, wherein the cells are selected from the group consisting of fibroblasts, endothelial

cells, chondrocytes, neuroblastoma cells, kidney cells, liver cells, pancreatic cells, thyroid cells, glial cells, smooth muscle cells, bone/cartilage forming cells, and any combination thereof.

49. The method of Claim 47, wherein the suspension is applied to the surface of the prosthetic device by fibrin glue.